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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,921	10/31/2005	Hiroshi Miura	280271US0X PCT	2311

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EXAMINER	
PALENIK, JEFFREY T	
ART UNIT	**PAPER NUMBER**
1615	

NOTIFICATION DATE	DELIVERY MODE
04/25/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/554,921	MIURA ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *31 Jan 2006 and 26 Sept 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Remarks

Applicant's election **without traverse** of Group I, claims 21-24, in the reply filed on 24 March 2008 is acknowledged.

Claims 25-35 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 24 March 2008.

The remaining claims 21-24 are presented and represent all claims under consideration.

Information Disclosure Statement

Two Information Disclosure Statements filed 31 January 2006 and 26 September 2007 are acknowledged and have been reviewed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21-24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 8, 11 and 12 of copending Application No. 10/551,901. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of the '901 application, like claim 21 of the instant application, is drawn to a composition comprising a very low (e.g. an extremely poorly) water-soluble drug. Both the claims are drawn only to the composition since the language in both claims reflects "product-by-process" language (see MPEP 2113). Co-pending claim 8 recites a range for the specific surface area which overlaps that which is recited in the instant claim 22. Instant claim 23 and co-pending claim 11 recite the same ratio of porous material to drug. Instant claim 24 and co-pending claim 12 both recite the compound 2-benzyl-5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "extremely poorly" in claims 21, 23 and 24, is a relative term which renders the claims indefinite. The term "extremely poorly" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The limitation rendered indefinite by the use of the above term, within the claim, is the degree of solubility of the drug. Given its broadest reasonable interpretation and for the purposes of examination on the merits, the limitation "extremely poorly water-soluble drug" is interpreted by the Examiner to mean "hydrophobic drug."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohkuchi et al. (U.S. Patent 6,348,468).

The instant claims 21, 22 and 23 are drawn to a composition comprising a hydrophobic drug. Per MPEP 2113, the recited claim language "obtained by treating…" defines the claim as a product-by-process claim. As such, the instant claim 21 is interpreted by the Examiner to read

only on the composition which is obtained regardless of the means through which it is obtained (i.e. composition comprising a hydrophobic drug). Dependent claims 22 and 23 both recite limitations to the process limitation of the instant claim 21 and *not* the resulting product or composition portion of the claim. As such, claims 22 and 23 are interpreted by the Examiner as reading on the same composition of claim 21. Dependent claim 24 further limits the hydrophobic drug of claim 21, specifically to 2-benzyl-5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one.

Ohkuchi et al. teaches in claim 8 a pharmaceutical composition comprising the hydrophobic compound: 5-(4-chlorophenyl)-6-(4-methylthiophenyl-2-benzyl-2H-pyridazin-3-one.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mandel et al. (WO 02/20624) in view of Tsutomu et al. JP-2002-345940 (machine translation), Ohkuchi et al. (U.S. Patent 6,348,468) and in further view of defined products available from Sigma-Aldrich.

The instant claims are drawn to a composition comprising a hydrophobic drug, as described above.

Mandel et al. teach a biologically active agent, which is treated with a supercritical fluid, being mixed with silicon-based polymeric particles. The biologically active agent is taught to be an immune-response modulator or a drug used in immunological products and/or vaccines (claim 7) and the porous particles are taught as being composed of silicon-based, thermoplastic and/or thermoset polymers such as polydimethylsiloxane or polyurethane (claims 8 and 9). Claim 1, 3, 4 and 29-33 teach a pharmaceutical mixture containing a biologically active ingredient, which has been treated with a supercritical fluid carbon dioxide, contained within engineered porous polymer particles.

Mandel et al. does not teach that the selected immunologically-based drug is necessarily hydrophobic (e.g. extremely poorly water soluble) or that it is the compound 5-(4-chlorophenyl)-6-(4-methylthiophenyl-2-benzyl-2H-pyridazin-3-one. It also lacks teachings for: a.) the specifics of the polymer particles (e.g. pore size, specific surface area), b.) that the porous material is porous *silica* material, or c.) the range of mixture ratios of porous silica material to hydrophobic drug.

Tsutomu et al. teach a sustained release material, treated (e.g. constituted) through supercritical or subcritical fluid, which is released from a porous material (claim 1). Claims 3-5

teach a porous silica body, which can carry a hydrophobic, sustained release material (e.g. an oil), which has been contacted by either a supercritical or subcritical fluid. Said fluid is taught as being carbon dioxide (claim 7).

Tsutomu et al. also does not teach the compound of the instant claim 24. It also lacks teachings for the specifics of the polymer particles (e.g. pore size, specific surface area) and the range of mixture ratios of porous silica material to hydrophobic material.

The teachings of Ohkuchi et al. are discussed above.

What is lacking is a teaching that treats the hydrophobic compound of Ohkuchi with a super- or subcritical fluid in addition to mixing it with the porous silica material. The specifics of the porous silica material used in the silica gel chromatography column and the ratio of the porous silica material to the hydrophobic drug are not taught.

In view of the combined teachings of the prior art, one of ordinary skill in the pharmaceutical or biomedical devices art would have been motivated to prepare a composition comprising porous silica particles or a porous silica material in combination with a hydrophobic material that had been treated with either super- or subcritical fluid with a reasonable expectation of successfully obtaining an infused pharmaceutical composition comprising said particles and the hydrophobic compound: 2-benzyl-5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one. Such would have been obvious in the absence of evidence to the contrary since Mandel and Tsutomu both teach treating compounds with supercritical liquid carbon dioxide and then mixing their respective compounds with porous silicon- or silica-based particles. Compounds which are treatable with the supercritical carbon dioxide prior to particle infusion, such as in the case of Mandel, can be both immunologically-based and hydrophobic, just like the

compound of Ohkuchi et al. and the instant claim 24. Tsutomu directly teaches in the claims, mixing hydrophobic material, which has been treated with supercritical carbon dioxide, with porous silica material.

None of the references teach the ratio of the porous silica material to hydrophobic drug nor do they teach the specific parameters of the porous silica material (e.g. pore size, specific surface area), as claimed by Applicants. Since the values of each parameter with respect to the claimed composition is adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to acquire silica gel column chromatography material having the requisite pore diameter (e.g. between 1-20 nm) and specific surface area (e.g. between 100-2,000 m^2/g) in addition to determining the optimal manufacturing method (e.g. ratio of porous silica material to hydrophobic drug) and/or specific surface area of the porous silica material) in order to best achieve the desired results (see Sigma-Aldrich silica gel product #403653). Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicant's invention.

No claims allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/Michael P Woodward/
Supervisory Patent Examiner, Art Unit 1615